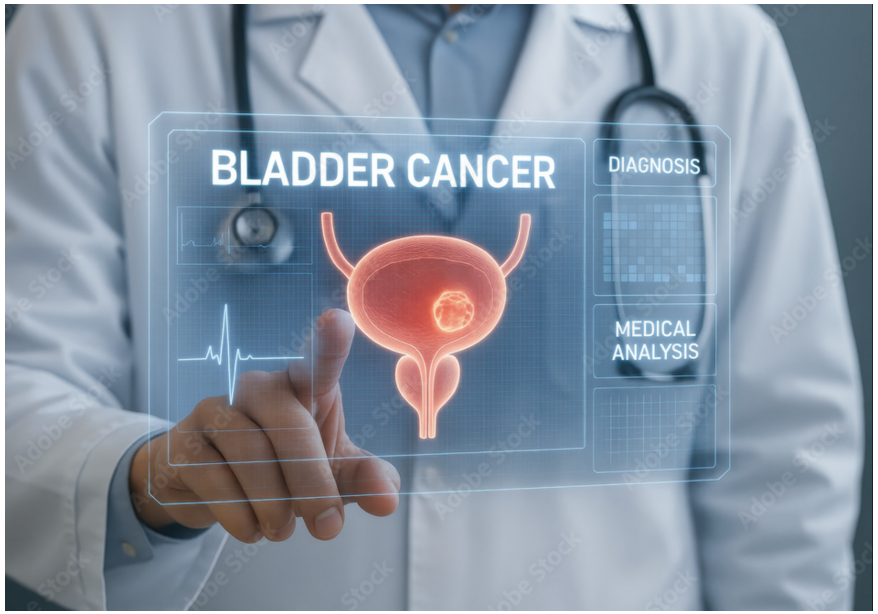
MasterClass in Bladder Cancer 2026

June 9th #BladderMasterClass26

Centro de Formación y Simulación Avanzada,
Hospital Universitario 12 de Octubre
Avda. de Córdoba, s/n. Madrid

Hospital Universitario 12 de Octubre



Systemic immunotherapy is the future

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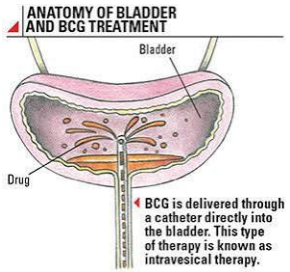
Editor-in-Chief, Actas Urológicas Españolas

The Begining of the End for BCG Monotherapy

Challenges of Administration

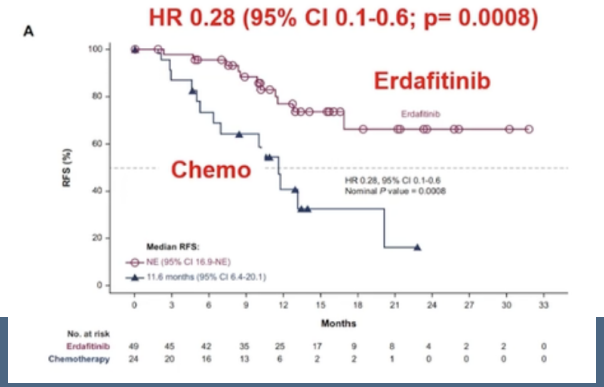
- General side effects
- Intolerance in 5%
- Dwell Time
- Treatment intensity



Oddens et al, Eur Urol 2013 Mar;63(3):462-72

A targeted agent Will Drive Precisión Care

- THOR 2: Cohort 1 (n=73): (Erdafitinib vs IV Chemo)
- HR 0.28(95% CI 0.1-0.6; p=0.0008)

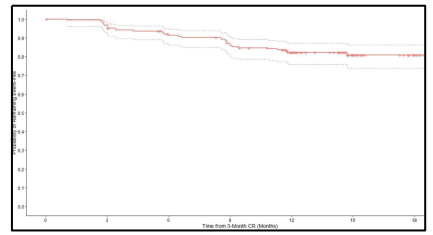


Catto et al. Annals of Oncology 35(1);98-106,2024

BCG Will Face Increased Competition in IR NMIBC

- UGN-102 ENVISION Trial
- Phase 3, single-arm 240 patients with LG-IR-NMIBC
- Participants received six weekly bladder instillations
- Efficacy and safety of UGN-102 as a primary chemoablative therapy using a MMC-containing reverse thermal gel

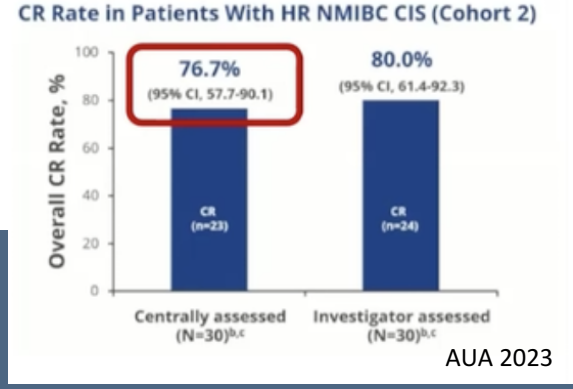
- CR at 3 months: 79.6%
- DOR at 12 months: 82.3%



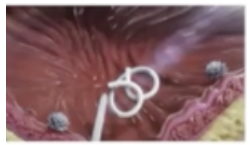
Prasad et al, J Urol 2025

Novel Agents are Improving Drug Delivery Over BCG

- Sunrise 1 Phase 2b Randomized Trial
- CR rate in patients with HR NMIBC CIS (Cohort 2)



AUA 2023



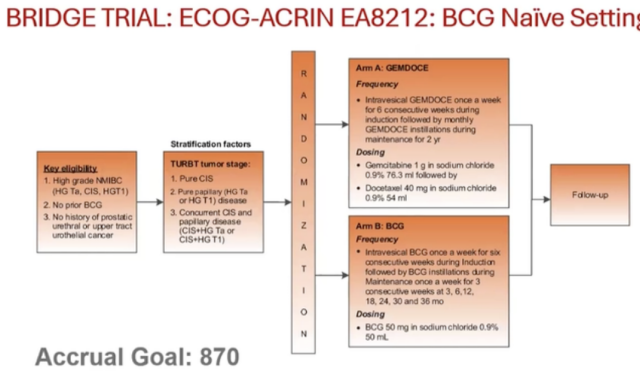
Low toxicity

The Begining of the End for BCG Monotherapy(II)

BCG Shortage

- Many urologist have had limited access

Chemotherapy is Challenging BCG as Frontline



Kates et al Eur Urol Focus. 9(4):561-563, 2023

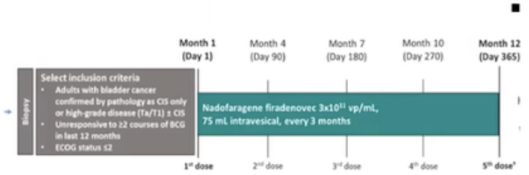
Combination BCG+IO Trials

- Crest, Potomac, Alban, Keynote 676

	Agent	Study Size	Eligible Population	Study Design
CREST	Sasanlimab	1070	Event Free Surv	Cohort 1: Sasanlimab + BCG (IND + MAIN) vs BCG (IND + MAIN) alone
POTOMAC	Durvalumab+ BCG	1300	Dis Free Surv	Durvalumab+BCG (IND+MAIN) vs Durv+BCG (IND) vs BCG (IND+MAIN)
KEYNOTE-676	Pembro + BCG	1405	Event Free Surv	Cohort 1: BCG-P vs BCG Cohort 2 BCG-P (Full vs Reduced MAIN) vs BCG monotherapy
ALBAN	Atezolizumab + BCG	516	Rec Free Surv	BCG + Atezolizumab vs BCG [IND/ MAIN for all)

Novel Agents Have More Convenient Treatment Schedules Than BCG

- BCG Unresponsive setting
- Nadofaragene Firadenovec
- HR-RF (57 mo. F/U; CIS: 5.8%; no CIS: 13%)
- 5-year CFS: CIS:43%: no CIS : 59%

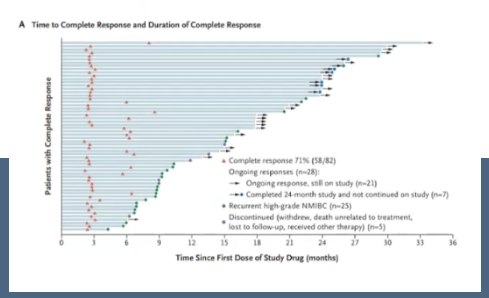


Dosed intravesically
q3months X 5

Boorjian, JCO 2020;38:442

Novel Agents are Synergistic with BCG

- Quilt-3.032: BCG+ALT-803(N-803)
- CR; 71% (Cohort A); DOR>12mo. 61,6%



Chamie et al; NEJM 2023; 2(1)

Why Do We Conduct Clinical Trials?

- To determine whether a treatment is safe and effective
- To compare new interventions with current standards of care
- To improve patient outcomes and quality of life
- To generate high-quality scientific evidence
- To guide clinical practice and healthcare decisions
- To advance medical knowledge and innovation

Clinical Trials: HR-NMIBC BCG naïve:Design

ALBAN – Study design

BCG-naive patients, with high-risk NMIBC after first and second look TURBT:

- High-risk defined as the presence of any high-grade/grade 3 Ta, T1 tumors and/or CIS
- No prior BCG therapy
- Absence of metastatic disease in the pelvis, abdomen, or chest
- ECOG PS of 0-2

R 1:1

BCG : once a week for 6 weeks (induction phase)
once a week for 3 weeks at 3, 6, 12 months (maintenance phase)

Atezolizumab: 1200 mg; IV; q3w for up to 1 year

BCG : once a week for 6 weeks (induction phase)
once a week for 3 weeks at 3, 6, 12 months (maintenance phase)

Primary endpoint
EFS

Key secondary endpoints
High-grade RFS
PFS
OS
DOR
Safety
QoL

CIS: carcinoma in situ; DOR, duration of response; EFS: Event-Free Survival; OS, Overall Survival; PFS: Progression-Free survival; QoL, Quality of Life; RFS: Recurrence-Free Survival

Patient Population:

- BCG-naive, high-risk NMIBC: T1, high-grade Ta, and/or CIS

(≥3 cm)

N=1055

Randomization

Arm A

Sasanlimab + BCG-Induction + Maintenance (I+M)

Arm B

Primary endpoint
EFS: A vs C
(recurrence of high-grade disease, progressive disease, persistence of CIS, death from any cause)

Key secondary endpoints

- Safety
- EORTC QLQ-C30

BCG (I+M)
N=340

BCG Induction	BCG Maintenance (3 weekly doses at)				
Weekly × 6 weeks[b]	3m	6m	12m	18m	24m

Shore ND et al, Nat Med 2025; De Santis M et al, Lancet 2025; Rouprêt M et al, Ann Oncol 2025

Clinical Trials: HR-NMIBC BCG naïve:Design and Results

Parameter	CREST	POTOMAC	ALBAN
Start date	December 2019	May 2018	January 2019
Completion date	December 2024	April 2025	June 2025
Locations	US, Canada, WU, Asia, Aus	WU, Asia, Aus	France, Belgium, Spain
Central path review	Yes (retrospective)	Yes (retrospective)	Yes (retrospective)
Baseline T-stage	58% T1 / 15% Pure CIS	58% T1 / Pure CIS NR	39% T1 / 7% Pure CIS
Experimental ICI Treatment Duration (ICI + BCG [I+M])	24 months	12 months	12 months
Control BCG Treatment Duration (BCG [I+M])	24 months	24 months	12 months
Re-induction allowed	Yes (CIS and HG Ta)	Yes (CIS)	No (Maintenance allowed at 3m for CIS)
EFS / DFS Definition	High grade NMIBC; Persistent CIS at 6m; MIBC; mUC; Death	High grade NMIBC; Persistent CIS at 6m; MIBC; mUC; Death	High grade NMIBC; Low-grade NMIBC; Persistent CIS at 6m; MIBC; mUC; UTUC any grade; Death
Targeted / Actual HR (ICI + BCG vs BCG)	0.69 / 0.68	0.63 / 0.68	0.63 / 0.98
Projected / Actual BCG Control	Median EFS 24m / NR	24m DFS 71% / 82%	24m EFS 70% / 75%

Shore ND et al, Nat Med 2025; De Santis M et al, Lancet 2025; Rouprêt M et al, Ann Oncol 2025

Clinical Trials: HR-NMIBC BCG naïve: Levels of Evidencie

CREST & POTOMAC	ALBAN
Higher-risk HR-NMIBC population (≈58% T1)	**Lower-risk HR-NMIBC population** (≈39% T1)
Full/relevant BCG maintenance duration in the control arm	Truncated BCG maintenance duration in the control arm
Demonstrated **EFS/DFS benefit** with ICI + BCG	**No EFS benefit** observed
Clinical question: *Does adding ICI to adequate BCG improve outcomes in higher-risk patients?*	Clinical question: *Does adding ICI to truncated BCG improve outcomes in lower-risk patients?*
Answer: YES ✓	**Answer: NO** ✗

Shore ND et al, Nat Med 2025; De Santis M et al, Lancet 2025; Rouprêt M et al, Ann Oncol 2025

Impact of Recurrence events in NMIBC

Additional BCG-Unresponsive Treatments

- Gemcitabine/Docetaxel
- Nadofaragene firadenovec
- Nogapendekin alfa inbakicept(NAI)+BCG
- HIVEC
- Pembrolizumab

Additional procedures

- Cistoscopies q/3mo.
- TURBTs /RB

Cystectomy

Urinary symptoms /QoL

Cost

Summary of evidence - treatment failure of intravesical therapy

Summary of evidence	LE
Prior intravesical chemotherapy has no impact on the effect of BCG instillation.	1a
Treatments other than RC must be considered oncologically inferior in patients with BCG-unresponsive tumours.	3

eau Guidelines

Patient Views on Bladder Preservation

Clinical-Bladder cancer

Patient experience and unmet needs in high-risk nonmuscle-invasive bladder cancer: Insights from qualitative interviews and a cross-sectional survey

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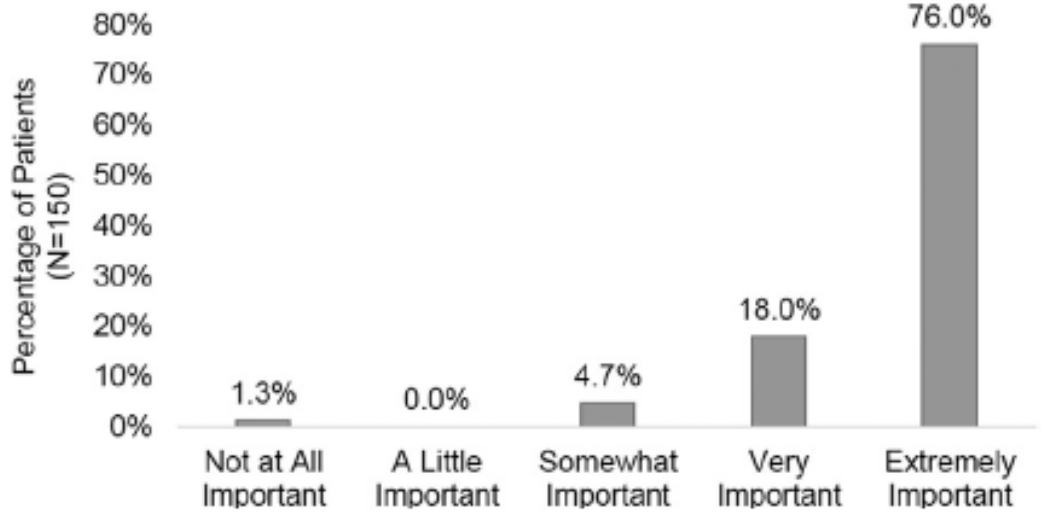

Fig. 2B. Importance of being able to keep bladder and avoid radical cystectomy – Phase 2: Quantitative survey.

Impact of ICI Toxicity

	CREST S + BCG (I+M)	CREST BCG (I+M)	POTOMAC D + BCG (I+M)	POTOMAC BCG (I+M)	ALBAN A + BCG (I+M)	ALBAN BCG (I+M)
Any Grade 3–4 AE	49%	26%	34%	17%	40%	24%
Treatment-Related Adverse Events (TRAEs) Gr 3–4	29%	6%	21%	4%	23%	9%
Immune-Related Adverse Events (irAEs) Gr 3–4	16%	0%	8%	<1%	6%	1%
Corticosteroid Use	20%	<1%	16%	<1%	NR	NR
Discontinuation of Study Treatment Due to TRAE	26%	9%	27%	17%	29%	9%
TRAE Death	0%	0%	0%	0%	0%	0%

Shore ND et al, Nat Med 2025; De Santis M et al, Lancet 2025; Rouprêt M et al, Ann Oncol 2025

Key Considerations in High-Risk NMIBC Treatment Decisions

Optimal care in high-risk NMIBC requires a multidimensional, patient-centered approach tailored to each individual.

Take-Home Messages

1. Level 1 Evidence Supports BCG + Immunotherapy
High-quality randomized evidence now supports the addition of **immune checkpoint inhibitors (ICI)** to intravesical **BCG** in patients with **BCG-naïve high-risk NMIBC**.

2. Clinical Benefit Outweighs the Added Toxicity in Selected Patients
The addition of ICI to BCG provides a **meaningful clinical benefit**, particularly in patients at the **highest risk of recurrence, progression, and metastasis**, while maintaining an **acceptable safety profile**.

3. Treatment Decisions Should Be Individualized
Optimal management requires **shared decision-making**, integrating:
- Disease risk
- Expected efficacy
- Toxicity profile
- Patient preferences and quality of life
- Treatment burden and access

Conclusion: BCG+IO is the logical step for shared decision making with HR-NMIBC patients

Thank You !!

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